



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#10
8-12-02

In re the application of: Bujard, Hermann *et al.*

Serial No.: 09/921,650

Filed: August 3, 2001

For: "Tetracycline-Inducible Transcriptional Inhibitor Fusion Proteins" (as amended)

Attorney Docket No.: BBI-009C6CNDVCN

Group Art Unit: 1631

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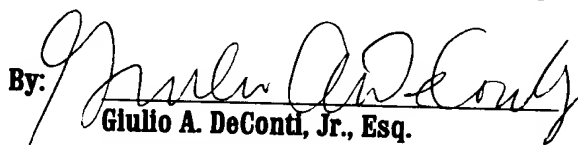
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By: 
Giulio A. DeConti, Jr., Esq.
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Attorney for Applicants

INFORMATION DISCLOSURE STATEMENT

Dear Sir:

Applicants and their Attorney are aware of the following patents, publications or other information, which are cited on the attached PTO Form 1449, and in accordance with 37 CFR §1.97 hereby submit these forms for the Examiner's consideration.

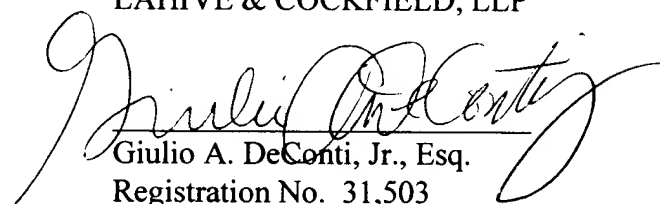
The present application is a continuation of U.S. Serial No. 09/489,777, filed January 24, 2000 (Atty. Docket No. BBI-009C6CNDV). All references listed on the enclosed PTO Form 1449 have been previously cited by or submitted to the Office

in the prior application, and, in accordance with 37 CFR §1.98(d), copies of these references are not enclosed herewith, but will be provided upon request.

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, Applicants understand that the Examiner will make an independent evaluation of the cited publications.

Under 37 CFR § 1.97(b)(3), no additional costs are believed to be due in connection with the filing of this disclosure. If, however, a first Office Action on the merits issues in this application bearing a mailing date prior to the date of this Information Disclosure Statement, please charge the appropriate fee as required under 37 CFR §1.17(p) to our Deposit Order Account No. 12-0080.

Respectfully submitted,
LAHIVE & COCKFIELD, LLP


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Date: July 31, 2002

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Re: U.S. Patent Application No.: 09/921,650
"Tetracycline-Inducible Transcriptional Inhibitor Fusion Proteins" (as amended)
Inventors: Bujard, Hermann *et al.*
Filed: August 3, 2001
Our Ref. No.: BBI-009C6CNDVCN

Dear Sir:

I enclose herewith for filing in the above-identified application the following:

1. Information Disclosure Statement;
2. PTO Form 1449; and
3. A Return Postcard.

No additional costs are believed to be due in connection with the filing of this Information Disclosure Statement. However, please charge any necessary fees in connection with the enclosed statement to our Deposit Order Account No. 12-0080. For this purpose, a duplicate of this sheet is attached.

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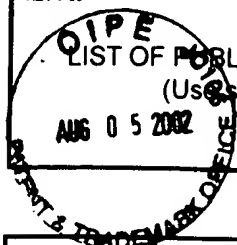
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Giulio A. DeConti, Jr., Esq., Registration No. 31,503

Respectfully submitted,
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Giulio A. DeConti, Jr., Esq.
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U.S. PATENT DOCUMENTS

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
AA	5,211,778	6/93	Byrne et al.	800	2	
AB	4,833,080	5/89	Brent et al.	435	172.3	

FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES NO
AC	WO 94/18317	08/94	PCT			
AD	WO 94/04672	03/94	PCT			
AE	WO 93/23431	11/93	PCT			
AF	WO 93/04169	03/93	PCT			
AG	WO 92/20808	11/92	PCT			
AH	WO 92/11874	07/92	PCT			
AI	0 494 724 A2	07/92	EPO			
AJ	WO 91/19796	12/91	PCT			
AK	WO 91/19784	12/91	PCT			
AL	0 455 687 B1	11/91	EPO			
AM	0 455 424 A3	11/91	EPO			
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AO	Ackland-Berglund, C.E. and Leib, D.A. (1995) "Efficacy of Tetracycline-Controlled Gene Expression Is Influenced by Cell Type" <i>BioTechniques</i> 18(2):196-200;
AP	Agarwal, M.L. et al., "p53 Controls Both the G ₂ /M and the G ₁ Cell Cycle Checkpoints and Mediates Reversible Growth Arrest in Human fibroblasts," <i>Proc. Natl. Acad. Sci. USA</i> , 92: pp. 8493-8497 (1995);
AQ	Altschmied, L. et al., (1988) "A threonine to alanine exchange at position 40 of Tet repressor alters the recognition of the sixth base pair of tet operator from GC to AT", <i>The EMBO Journal</i> , 7(12):4011-4017;
AR	Baim, S.B., et al., (1991) "A chimeric mammalian transactivator based on the lac repressor that is regulated by temperature and isopropyl β-D-thiogalactopyranoside", <i>Proceedings of the National Academy of Science</i> 88: 5072-5076;
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

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BA	Baniahmad, A. et al. (1992) "A Transferable Silencing Domain Is Present In the Thyroid Hormone Receptor, In the v-erbA Oncogene Product and In the Retinoic Acid Receptor" <i>The EMBO Journal</i> 11(3):1015-1023;
BB	Bergman, M. et al. "Overexpressed Csk Tyrosine Kinase Is Localized in Focal Adhesions, Causes Reorganization of $\alpha_v\beta_5$ Integrin, and Interferes with HeLa Cell Spreading", <i>Molecular and Cellular Biology</i> , 15, No. 2, pp. 711-722 (1995);
BC	Boshart, M., et al., (1985) "A Very Strong Enhancer Is Located Upstream of an Immediate Early Gene of Human Cytomegalovirus", <i>Cell</i> 41(2):521-530;
BD	Bradley, A., (1991) "Modifying the mammalian genome by gene targeting", <i>Current Opinion in Biotechnology</i> 2: 832-829;
BE	Brent, R. and M. Ptashne (1984) "A Bacterial Repressor Protein or a Yeast Transcriptional Terminator Can Block Upstream Activation of A Yeast Gene" <i>Nature</i> 312:612-615;
BF	Brent R. and M. Ptashne (1985) "A Eukaryotic Transcriptional Activator Bearing the DNA Specificity of a Prokaryotic Repressor" <i>Cell</i> 43:729-736;
BG	Brown, M., et al., (1987) "lac Repressor Can Regulate Expression from a Hybrid SV40 Early Promoter Containing a lac Operator in Animal Cells", <i>Cell</i> . 49:603-612;
BH	Buckbinder L. et al. (1994) "Gene Regulation by Temperature-Sensitive p53 Mutants: Identification of p53 response genes" <i>Proc. Natl. Acad. Sci. USA</i> 91:10640-10644;
BI	Capecchi, M.R., (1989) "Altering the Genome by Homologous Recombination", <i>Science</i> 244:1288-1292;
BJ	Cayrol, C. et al. "Identification of Cellular Target Genes of the Epstein-Barr Virus Transactivator Zta: Activation of Transforming Growth Factor β h3 (TGF- β h3) and TGF- β 1", <i>Journal of Virology</i> , 69, No. 7, pp. 4206-4212, (1995);
BK	Chen, Y.Q. et al. "Tumor Suppression by p21 ^{WAF1} ", <i>Cancer Research</i> , 55, pp. 4536-4539, (1995);
BL	Courey, A.J., and Tjian, R., (1988) "Analysis of Sp1 <i>In Vivo</i> Reveals Multiple Transcriptional Domains, Including a Novel Glutamine-Rich Activation Motif", <i>Cell</i> 55:887-898;
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BO	Degenkolb, J. et al. "Structural Requirements of Tetracycline-Tet Repressor Interaction: Determination of Equilibrium Binding Constants for Tetracycline Analogs with the Tet Repressor" <i>Antimicrobial Agents and Chemotherapy</i> 35(8):1591-1595 (1991);
BP	Deuschle, U., et al., (1989) "Regulated expression of foreign genes in mammalian cells under the control of coliphage T3 RNA polymerase and lac repressor", <i>Proceedings of the National Academy of Science</i> 86:5400-5404;
BQ	Deuschle et al., "Tetracycline-reversible silencing of eukaryotic promoters," <i>Mol. Cell. Biol.</i> , 15:4, 1907-1914 (1995);
BR	Dhawan, J. et al. "Tetracycline-Regulated Gene Expression Following Direct Gene Transfer into Mouse Skeletal Muscle", <i>Somatic Cell and Molecular Genetics</i> , 21, No. 4, pp. 233-240, (1995);
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PA	Elrat, S. et al. "Conditional Transformation of a Pancreatic β -Cell Line Derived From Transgenic Mice Expressing A Tetracycline-Regulated Oncogene" <i>Proc. Natl. Acad. Sci. USA</i> , 92, pp. 3576-3580 (1995);
CB	Epstein-Baak, R., et al., (1992) "Inducible Transformation of Cells from Transgenic Mice Expressing SV40 under <i>Lac</i> Operon Control", <i>Cell Growth & Differentiation</i> 3:127-134;
CC	Fieck, A., et al., (1992) "Modifications of the <i>E. Coli</i> <i>Lac</i> Repressor for Expression in Eukaryotic Cells: Effect of Nuclear Signal Sequence on Protein Activity and Nuclear Documentation", <i>Nucleic Acid Research</i> 20:1785-1791;
CD	Figge, J., et al., (1988) "Stringent Regulation of Stably Integrated Chloramphenicol Acetyl Transferase Genes by <i>E. coli lac</i> Repressor in Monkey Cells", <i>Cell</i> 52:713-722;
CE	Fishman G. et al. (1994) "Tetracycline-Regulated Cardiac Gene Expression in Vivo" <i>J. Clin. Invest.</i> 93:1864-1868;
CF	Furth P. (1994) "Temporal Control of Gene Expression in Transgenic Mice By A Tetracycline-Responsive Promoter" <i>Proc. Natl. Acad. Sci. USA</i> 91:9302-9306;
CG	Gatz et al. "Stringent repression and homogeneous de-repression by tetracycline of a modified CaMV 35S promoter in intact transgenic tobacco plants," <i>The Plant Journal</i> , 2:3, 397-404 (1992);
CH	Gatz, C. et al. "Regulation of a modified CaMV 35S Promoter by the Tn 10-encoder Tet Receptro in Transgenic Tobacco" <i>Mol. Gen. Genet.</i> 227(2):229-237 (1991);
CI	Gatz, C. and P. Quail "Tn10-Encoded <i>tet</i> Repressor Can Regulate and Operator-Containing Plant Promoter" <i>Proc. Natl. Acad. Sci. USA</i> 85:1394-1397 (1988);
CJ	Gjerding, T. et al. "Regulated Expression of the Retinoblastoma Susceptibility Gene in Mammary Carcinoma Cells Restores Cyclin D1 Expression and G ₁ -Phase Control", <i>Biol. Chem. Hoppe-Seyler</i> , 376, pp. 441-446 (1995);
CK	Gossen M. and B. Hermann (1993) "Anhydrotetracycline, A Novel Effector of Tetracycline Controlled Gene Expression Systems In Eukaryotic Cells" <i>Nucleic Acids Research</i> 21(18):4411-4412;
CL	Gossen, M., et al., (1993) "Control of gene activity in higher eukaryotic cells by prokaryotic regulatory elements", <i>TIBS</i> 18(12):471-475;
CM	Gossen et al., "Exploiting prokaryotic elements for the control of gene activity in higher eukaryotics," Keystone Symposium on Gene Therapy and Molecular Medicine, Steamboat Springs, Colorado, <i>Journal of Cellular Biochemistry</i> , Supplement 0 (21A), Abstract no. C6-220, 355 (1995);
CN	Gossen et al. (1994) "Inducible Gene Expression Systems For Higher Eukaryotic Cells" <i>Current Opinion in Biotechnology</i> 5:516-520;
CO	Gossen, M., and Bujard, H., (1992) "Tight control of gene expression in mammalian cells by tetracycline-responsive promoters", <i>Proceedings of the National Academy of Science</i> 89:5547-5551;
CP	Gossen et al., "Transcriptional activation by tetracyclines in mammalian cells," <i>Science</i> , 268:5218, 1766-1769 (1995);
CQ	Haase, S.B. et al. "Transcription Inhibits the Replication of Autonomously Replicating Plasmids in Human Cells", <i>Molecular and Cellular Biology</i> , 14, No. 4, pp. 2516-2524 (1994);

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DA	Hecht, B., et al., (1993) "Noninducible Tet Repressor Mutations Map from the Operator Motif to the C Terminus", <i>Journal of Bacteriology</i> 175(4);
DB	Hennighausen, L. et al. "Conditional Gene Expression in Secretory Tissues and Skin of Transgenic Mice Using the MMTV-LTR and the Tetracycline Responsive System", <i>Journal of Cellular Biochemistry</i> , 59, pp. 463-472, (1995);
DC	Herschbach B. and A. Johnson (1993) "Transcriptional Repression In Eukaryotes" <i>Annu. Rev. Cell Biol.</i> 9:479-509;
DD	Hillen, W., and Schollmeier, K., (1983) "Nucleotide sequence of the Tn10 encoded tetracycline resistance gene", <i>Nucleic Acid Research</i> 11(2):525-539;
DE	Hinrichs, W., et al., (1994) "Structure of the Tet Repressor-Tetracycline Complex and Regulation of Antibiotic Resistance", <i>Science</i> 264:418-420;
DF	Howe, J.R. et al. "The Responsiveness of a Tetracycline-Sensitive Expression System Differs in Different Cell Lines", <i>The Journal of Biological Chemistry</i> , 270, No. 23, pp. 14168-14174, (1995);
DG	Hu, M.C-T and Davidson, N., (1987) "The Inducible <i>lac</i> Operator-Repressor System Is Functional in Mammalian Cells", <i>Cell</i> 46:555-566;
DH	Labow, M.A., et al., (1990) "Conversion of the <i>lac</i> Repressor into an Allosterically Regulated Transcriptional Activator for Mammalian Cells", <i>Molecular and Cellular Biology</i> 10(7):3343-3356;
DI	Liang et al., "Enhanced and switchable expression systems for gene-transfer," Keystone Symposium on Gene Therapy and Molecular Medicine, Steamboat Springs, Colorado, <i>Journal of Cellular Biochemistry</i> , Supplement 0 (21A), Abstract no. C6-220, 379 (1995).
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DK	Mansour, S.L. et al. "Disruption of the Proto-Oncogene <i>int-2</i> in Mouse Embryo-Derived Stem Cells: a General Strategy for Targeting Mutations to Non-Selectable Genes" <i>Nature</i> 336:348-352 (1988);
DL	Mermoud N. et al. "The Proline-Rich Transcriptional Activator of CTF/NF-1 Is Distinct from the Replication and DNA Binding Domain" <i>Cell</i> 58:741-753 (1989);
DM	Miller, K. et al. "The Function of Inducible Promoter Systems in F9 Embryonal Carcinoma Cells", <i>Experimental Cell Research</i> , 218, pp. 144-150, (1995);
DN	Passman, R.S. et al., "Regulated Expression of Foreign Genes In Vivo After Germline Transfer", <i>J. Clin. Invest.</i> , 94, pp. 2421-2425 (1994)
DO	Pescini R. et al. (1994) "Inducible Inhibition of Eukaryotic Gene Expression" <i>Biochemical and Biophysical Research Communications</i> 202(3):1664-1667;
DP	Postle, K., et al., (1984) "Nucleotide sequence of the repressor gene of the TN10 tetracycline resistance determinant", <i>Nucleic Acid Research</i> 12(12):4849-4863;
DQ	Renkawitz R. (1990) "Transcriptional Repression In Eukaryotes" <i>TIG</i> 6(6):192-193;
DR	Resnitzky D. (1994) "Acceleration of the G1/S Phase Transition by Expression of Cyclins D1 and E with an Inducible System" <i>Molecular and Cellular Biology</i> 14(3):1669-1679;

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EA	Sauer, F. and H. Jäckle (1993) "Dimerization and the Control of Transcription by Krüppel" <i>Nature</i> 364:454-457;
EB	Seipel, K., et al., (1992) "Different activation domains stimulate transcription from remote ('enhancer') and proximal ('promoter') positions", <i>The EMBO Journal</i> 11(13):4961-4968;
EC	Smithies, O., et al., (1985) "Insertion of DNA sequences into the human chromosomal β -globin locus by homologous recombination", <i>Nature</i> 317:pp. 230-234;
ED	Sopher, B.L. et al., "Cytotoxicity Mediated By Conditional Expression of a Carboxyl-Terminal Derivative of the β -Amyloid Precursor Protein", <i>Molecular Brain Research</i> , <u>26</u> , pp. 207-217, (1994);
EE	Tovar, K., et al., (1988) "Identification and nucleotide sequence of the class E <i>tet</i> regulatory elements and operator and inducer binding of the encoded purified Tet repressor", <i>Mol. Gen. Genet.</i> 215:76-80;
EF	Triezenberg, S.J., et al., (1988) "Functional dissection of VP16, the <i>trans</i> -activator of herpes simplex virus immediate early gene expression", <i>Genes & Development</i> 2:718-729;
EG	Unger, B., et al., (1984) "Nucleotide sequence of the gene, protein purification and characterization of the pSC101-encoded tetracycline resistance-gene-repressor", <i>Gene</i> . <u>31</u> :103-108;
EH	Unger, B., et al., (1984) "Nucleotide sequence of the repressor gene of the RA1 tetracycline resistance determinant: structural and functional comparison with three related Tet repressor genes", <i>Nucleic Acid Research</i> 12(20):7693-7703;
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EJ	Weinmann P. et al. (1994) "A Chimeric Transactivator Allows Tetracycline-Responsive Gene Expression in Whole Plants" <i>The Plant Journal</i> 5(4):559-569;
EK	Wimmel A. et al. (1994) "Inducible Acceleration of G1 Progression Through Tetracycline-Regulated Expression of Human Cyclin E" <i>Oncogene</i> 9:995-997
EL	Wissmann, A. et al. "Selection for Tn10 Tet Repressor Binding to <i>tet</i> Operator in <i>Escherichia coli</i> : Isolation of Temperature-Sensitive Mutants and and combinatorial Mutagenesis in the DNA Binding Motif" <i>Genetics</i> 128:225-232 (1991);
EM	Wu, Z. et al. "Conditional Ectopic Expression of C/EBP β in NIH-3T3 Cells Induces PPAR γ and Stimulates Adipogenesis", <i>Genes & Development</i> , 9, pp. 2350-2363, (1995).
EN	Wyborski, D.L., and Short, J.M., (1991) "Analysis of Inducers of the <i>E. Coli</i> Lac Repressor System in Mammalian Cells and Whole Animals", <i>Nucleic Acid Research</i> 19:4647-4653;
EO	Yarranton G. (1992) "Inducible Vectors For Expression In Mamalian Cells" <i>Current Opinion in Biotechnology</i> 3:506-511.

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